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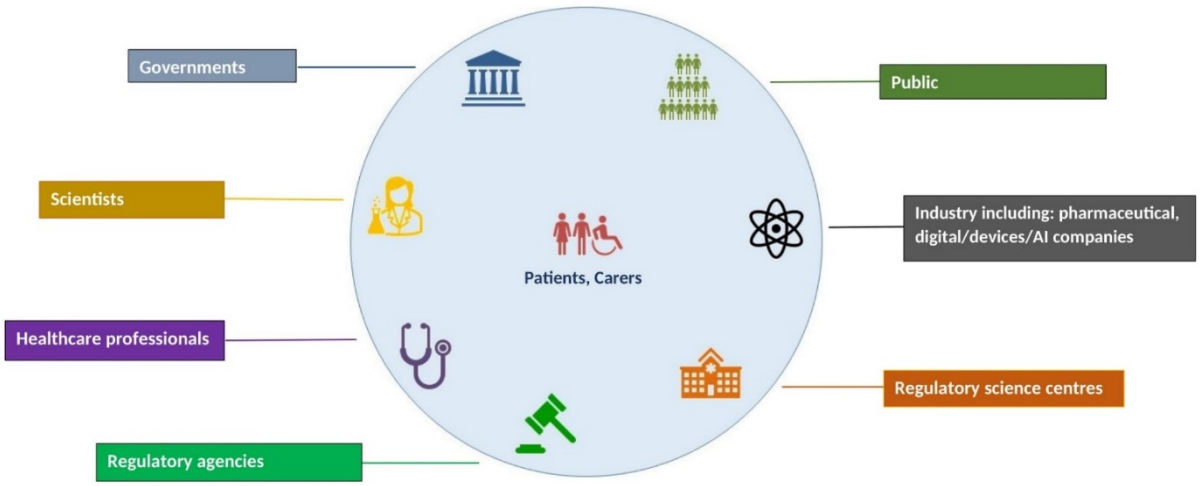
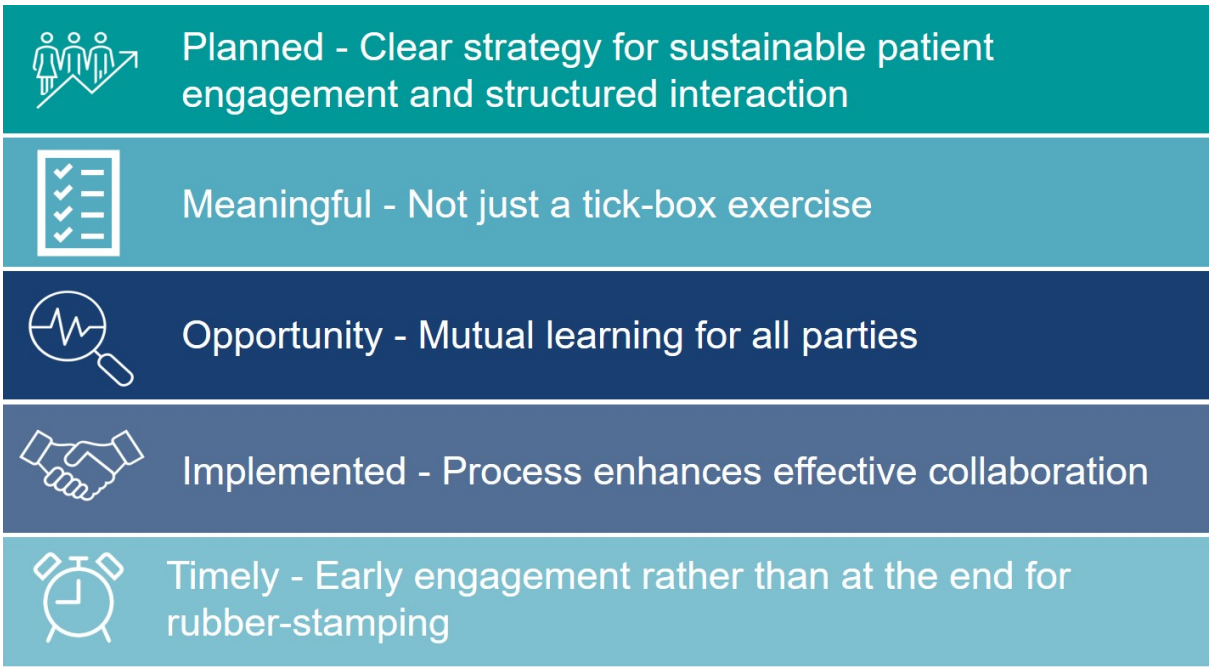
Supplementary information

The opportunity for greater patient and public involvement and engagement in drug development and regulation

In the format provided by the authors



Supplementary Figure 1 | Key stakeholders in regulatory science and processes.



Supplementary Figure 2 | Elements of PPIE, proposed by Kathy Oliver, Patient Advocate and Chair of IBTA.

Supplementary Box 1 | Definition of key terms

Regulatory science in healthcare has been defined as "the range of scientific disciplines that are applied to the quality, safety, and efficacy assessment of medicinal products and that inform regulatory decision-making throughout the lifecycle of a medicine. It encompasses basic and applied biomedical and social sciences and contributes to the development of regulatory standards and tools."[1] Regulatory science can also be applied in broader contexts such as medical device regulation. Regulatory science underpins the work of regulatory agencies, scientists, manufacturers, healthcare professionals, and other expert stakeholders.

The **'involvement'** component of PPIE refers to activities and research carried out 'with' or 'by' members of the public or patients, rather than 'to', 'about' or 'for' them. Patients and members of the public are actively involved in the development, running and management of regulatory science research projects or activities contributing to the advancement of regulatory standard and tools.[2,3]

The **'engagement'** element focuses on the dissemination of information and outcomes from research or regulatory activities to patients and the public, so that they are informed of developments while providing them the opportunity to share their insights and input.[2,3]

Supplementary Box 2 | Examples of PPIE initiatives by regulators

FDA

- The Patient Representative Program is one of the avenues for recruiting patients and caregivers with lived experiences of a condition, or medical device.
- Patient Engagement Advisory Committee (PEAC) ensures that patients' needs, and experiences are incorporated in FDA's considerations on the regulation of medical devices.
- Patient Engagement Collaborative (PEC) is a patient group that focuses on enhancing patient engagement in medical product development and regulatory discussions at FDA.
- Patient and Caregiver Connection (PCC), provides access to patient and carer experiences through patient organisations on behalf of Center for Devices and Radiological Health (CDRH).
- CDRH-sponsored Community Town Hall meetings discuss a broad range of topics including medical conditions and devices.
- Patient Group Conversations involve patients and/or representatives of patient groups discussing their condition and experiences with CDRH staff.
- Office of Patient Affairs manages the Patient Listening Sessions, these can be FDA-requested or patient-led.
- Multidisciplinary Public Health Symposiums that include subject experts and patients
- The FDA collaborates with academia through Centres of Excellence in Regulatory Science and Innovation (CERSIs) and Broad Agency Announcements to advance regulatory science through innovative research, training, and scientific exchanges.
- FDA and EMA also collaborate on patient engagement through the FDA/EMA Patient Engagement Cluster.

EMA

- Representatives of patient organisations - The Council of the EU appoints these representatives for 3-year terms on EMA's Management Board. These individuals contribute to the Board's activities, including the supervision of budgets, operational tasks such as the adoption of legally binding implementation rules, setting strategic directions for scientific networks, and reporting the utilisation of EU contributions for the Agency's activities.

- Patient representatives are also members and alternates in four scientific committees namely the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT) and the Pharmacovigilance and Risk Assessment Committee (PRAC). They are appointed by the European Commission, where they are systematically involved in the core business of regulating the development, approval, and supervision of medicines.
- Patient representatives of their own organisation - Representatives of patients and consumers organisations are also members of EMA's Patients and Consumers Working Party (PCWP), which provides a forum for the agency to obtain the input of these stakeholders.
- Representatives from patient organisations are also proactively involved in EMA's public consultations and workshops.
- Patients as individual experts - EMA also systematically seeks the input of individual patients, via its network of eligible organisations and its database of individuals, to ensure that their lived experiences are considered during EMA's evaluations. Patients are also observers of other aspects of the Agency's work.

MHRA

- The MHRA's Patient Group Consultative Forum is a large pool of patients, their caregivers, patient groups and the public that the agency engages and involves in many aspects of its work. The forum is open to individual interested in medicines and medical devices and currently has over 180 participants. Participants can attend subject-specific workshops, provide feedback on draft documents and participate in surveys that inform the agency's work.
- Patient and public representatives sit on expert panels established by the Commission on Human Medicines to advise on issues associated with access to medicines (through a doctor's prescription or over-the-counter from a pharmacy).
- The Valproate Stakeholders' Network (VSN) comprising of representatives from the MHRA, healthcare professional bodies, healthcare delivery organisations, patient groups, and research charities was established to capture public input for the regulation of sodium valproate.
- The Medicines in Pregnancy and Breastfeeding Consortium comprises of representatives from providers of information to women and healthcare professionals regarding medicines taken during pregnancy and breastfeeding.
- All of the agency's regular Board meetings are open to the public and include a dedicated session for public and patients to ask questions of the agency.
- The agency undertakes a large number of online consultations to inform policy development or to obtain a richer understanding of the patient perspective on a particular issue or topic.
- Expert panels with lay representation such as the Devices Expert Advisory Committee (DEAC) provides the agency with independent, input and advice on a wide range of aspects relating to the introduction and safe use of medical devices.

Health Canada

- Canada's Centre for Policy, Pediatrics and International Collaboration is developing a Patient Involvement Strategy with the goal of better integrating patient expertise into Health Canada's policy and regulatory decisions.
- Patient Listening Sessions, first piloted with the amyotrophic lateral sclerosis (ALS) community in Dec. 2021, provide an opportunity for to leverage patient knowledge and expertise in several policy and regulatory activities. Future listening sessions will build on the lessons learned during this pilot session.
- Patient advocates have been serving as members of Health Canada's standing Scientific and Expert Advisory Committees. Patient advocates, along with all other committee members, are educated on the regulatory process so that they may understand the scientific as well as the regulatory context within which Health Canada makes decisions.

Supplementary Box 3 | Case study of Guidelines developed by CRSI with PPIE input

Patient partners provided a worldview detailing their experiences and co-developed and co-authored the Standard Protocol Items: Recommendations for Interventional Trials - Artificial Intelligence (SPIRIT-AI)[4] and the Consolidated Standards of Reporting Trials - Artificial Intelligence (CONSORT-AI)[5] guidelines published in Nature Medicine, BMJ and Lancet Digital Health. Birmingham Health Partners CRSI collaborated with patients/patient experts, regulators, industry experts, and governmental bodies in the development of guidelines to enhance the development and regulation of medicines and medical devices.[6]

Patient involvement helped ensure the guidelines were clear and easy to implement. Input to this work was described by patient partner Elaine Manna in a Nature Medicine World View – "My disability has become an ability".[7]

Supplementary Box 4 | Practical considerations to facilitate PPIE activities

Co-organisation of activities - This may involve developing outreach programmes whereby agencies and existing patient partners co-organise "road show" activities, information days, and workshops within the underserved communities.

Accessibility and transportation - Consideration should be given to the choice of locations for in person meetings in terms of wheelchair access, and proximity to good transport links.

Reimbursement - Patient and public contributors should be reimbursed for their expenses and time commitment. Ideally, expenses directly incurred as a result of participating in research should be covered for clinicians and other collaborators and refreshments provided as required.

Inductions and training - Public contributors need to be supported in their involvement and should receive induction and training tailored to their needs and level of experience. The use of technical jargon should be avoided.

Flexibility - To encourage greater participation from a broad group of individuals, there is a need for flexibility in terms of the timing and location of meetings, and formats for participation (in person or online). Less formal venues may be used for consultations to encourage participation from all members of society.

References

1 EMA. Road map to 2015 - The European Medicines Agency's contribution to science, medicines and health. (2010).

2 NIHR. *What is Patient and Public Involvement and Public Engagement?* , <https://www.spcr.nihr.ac.uk/PPI/what-is-patient-and-public-involvement-and-engagement>

3 HDRUK. *Patient and Public Involvement and Engagement* <https://www.hdruk.ac.uk/about-us/patient-and-public-involvement-and-engagement/>

4 Cruz Rivera, S. *et al.* Guidelines for clinical trial protocols for interventions involving artificial intelligence: the SPIRIT-AI extension. *Nature Medicine* **26**, 1351-1363, doi:10.1038/s41591-020-1037-7 (2020).

5 Liu, X. *et al.* Reporting guidelines for clinical trial reports for interventions involving artificial intelligence: the CONSORT-AI extension. *Nature Medicine* **26**, 1364-1374, doi:10.1038/s41591-020-1034-x (2020).

6 Samuels, M., Marston, E. & Calvert, M. Advancing Regulatory Science and Innovation in Healthcare. (The Birmingham Health Partners Centre for Regulatory Science and Innovation (CRSI), 2020).

7 Manna, E. "My disability has become an ability". *Nature Medicine* **26**, 1317-1317, doi:10.1038/s41591-020-1053-7 (2020).